

November 13, 1950.

Dear Jacques:

By an amusing coincidence, we appear to have suffered simultaneously the attack of *Cacoethes Scribendi* which led to the crossing of our letters in the mail.

We have already had the pleasure of Bussard's acquaintance. I think your fears will be, happily, unfounded. After some initial difficulties in obtaining facilities in the Zoology Department, he has been able to begin to work. We hope to see him again often; our past contacts were very entertaining, and I can well appreciate your fondness for him.

We spent the summer at Berkeley, but unfortunately Doudoroff returned just as we left, and we did not have enough opportunity to talk with him.

As my previous letter indicated, my rather trite paper on galactosidase has just reached print in the October issue of *J. Bact.*, which should reach you at any moment. The paper mentions almost everything I have on the K-12 enzyme, including the metal effects. One of Dr. Lardy's students at the Enzyme Research Institute here has taken up the problem, with particular reference to the kinetics of formation of the enzyme-metal-substrate complex, with various substrates (but ONPG especially), and substituted ammonium salts as metal analogues as well. This is my only paper on the subject, but the multigenic control of lactase formation is mentioned in an abstract in *Genetics* (1948).

A propos your remark in one of your papers that there is no report that more than one gene controls the specific quality of an enzyme, may I ask what situation you have in mind for the effect of even one gene on such a quality? Thinking hypothetically of this problem, I have wondered how one could distinguish between a genetic effect on an enzyme quality and on the formation of an alternative protein with similar enzymatic action. I have some hopes that  $\lambda$  lactase from other strains, crossable with K-12, may provide material for such further studies.

I do not know whether my last letter mentioned some of Esther's latest results. Some of the "allelic" recurrences of Lac- mutation turn out, like lozenge in *Drosophila* (and "Q" in *Neurospora* - Bonner) to be "pseudo-allelic", i.e., cross over at extremely low frequencies (ca.  $10^{-4}$ ) to give Lac $\phi$ . These are now being studied in heterozygous compounds, but I have an indirect suspicion that, like lozenge, the "alleles" do not interact. Esther is more cautious and would prefer not to make a definite statement, but this is "off the record".

Please give Francis and Betty Ryan our best regards. I enjoyed his travel letters,

With hopes that we can take this opportunity to renew contacts,

Sincerely,

Joshua Lederberg